SECRETARY OF THE ARMY
WASHINGTON

MAY 29 2002

Honorable Bob Stump
Chairman
Committee on Armed Services
2120 Rayburn House Office Building
Washington, DC 20515-6035

Dear Chairman Stump:

House Report 107-350, p.425, directs the Secretary of the Army to conduct a feasibility study and submit a report on the expanded role of U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) to the congressional defense committees. The enclosed report will define the expanded USAMRIID mission, determine the infrastructure requirements, associated costs and describe the plan for implementation into the Future Years Defense Program (FYDP).

The report indicates that the current facilities and infrastructure will not meet USAMRIID's expanded mission requirements in a post September 11 environment. More advanced and larger laboratory facilities are required. A comparison of an addition/alteration versus replacement shows that a replacement facility at Fort Detrick is the most responsive and economical solution. An adequately sized replacement laboratory is estimated to cost $1.006 billion dollars including all associated costs. When and if funding is identified, the capital effort should be phased funded over a 5-year period with accelerated design and construction methods starting in FY 2003.

Respectfully,

Thomas E. White

Enclosure

Report to the Congress Concerning The Expanded Role and Mission of The U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) and Associated Infrastructure Requirements

Submitted by the Secretary of the Army
In Compliance with
House Report 107-350 p.425 dated 19 December 2001

1 May 2002

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Executive Summary

House Report 107-350, 19 December 2001, requested that the Secretary of the Army conduct a feasibility study and submit a report on the expanded role of the US Army Medical Research Institute of Infectious Diseases (USAMRIID), US Army Medical Research and Materiel Command, Ft. Detrick, Maryland.

The conclusion is that USAMRIID's mission requirements cannot be met in the present facility. A modern and larger high-containment laboratory facility or facilities are required. A comparison of two alternatives demonstrates that a replacement facility at Fort Detrick is the most operationally responsive and economical solution. An adequately sized replacement laboratory is estimated at $1.006 billion including associated planning, design, environmental analysis, support infrastructure, building construction, transition, outfitting and commissioning costs. More detailed information is available in the USAMRIID Master Plan Report. No funding is currently available to satisfy the requirement. The Army Surgeon General is currently developing a DD Form 1391, Military Construction Project Data.

This report describes the USAMRIID mission and infrastructure requirements, associated project costs, and a draft plan for implementation in a Future Years Defense Program (FYDP). It also articulates the critical role USAMRIID plays in meeting both traditional and new biological threats to support the nation's warfighters and the American people. The report further describes USAMRIID's unique organizational competencies and capabilities and its role in scientific collaboration with other federal agencies, academia, and industry. The report does not describe other potential alternatives to satisfy the requirement, nor describe acquisition execution methodologies or acquisition program management.

Because of its military mission, USAMRIID has distinctive capabilities that meet both the warfighting and homeland security challenges of the 21st century. USAMRIID is the only Level D Diagnostic Reference Laboratory in the DoD, one of two in the U.S. (CDC in Atlanta being the other). It has the only aerosol testing facilities in the U.S. Department of Defense for highly pathogenic agents with the ability to evaluate animals in research ranging from rodents to nonhuman primates. It also possesses the largest amount of Biological Safety Level 3 and 4 animal care facilities in the U.S. capable of supporting research and testing required for licensure of vaccines and other products that derive from the response to biological or other disease threats.

The findings are based on a facility master planning study commissioned by the Army Surgeon General, part of a larger Army-wide medical and research infrastructure recapitalization effort. The study analyzed the present and anticipated USAMRIID mission, documented facilities deficiencies, consolidated infrastructure and future mission requirements, and developed the requirement for a long-term, mission-based capital improvement program for USAMRIID.

1 Overview

This report responds to House Report 107-350, dated 19 December 2001, tasking the Secretary of the Army to conduct a feasibility study concerning the expanded role of U.S Army Medical Research Institute of Infectious Diseases (USAMRIID) in light of post 11 September 2001 events and to provide a report that:

Finalizes the expanded mission of the USAMRIID

- Determines the infrastructure requirements of USAMRIID
- Determines the associated costs

Describes a funding methodology for implementation in the Future Years Defense Program (FYDP).

The report findings are based on a US Army Surgeon General sponsored facility master planning study that analyzed the present and anticipated USARMIID mission requirements, documented facilities requirements, and consolidated and developed operationally-based infrastructure planning scenarios.

Prior to defining the scope of facilities infrastructure, USAMRIID's leadership and the master planning team developed and executed a strategic planning process to define the critical competencies and capacities USAMRIID must have to be successful over the next two decades. They developed a set of strategies that will be successful across a range of plausible futures, and developed a shared image (vision) of what USAMRIID should become. The effort examined external forces that are transforming national security strategy, new developments in global technological infrastructure, biotechnology and genomics convergence, and global population growth. The USAMRIID leadership systematically explored these forces of change and developed a set of strategies to meet the opportunities and challenges each of these forces imply. This report identifies the future threats that will have an impact on USAMRIID's mission and the roles that USAMRIID and other federal agencies are expected to play as part of a federal consortium in response to the need for medical research and development and for consequence management for the nation. These factors led to defining the future mission and organization of USAMRIID and the capabilities required to support it. This in turn led to defining the infrastructure required to support USAMRIID's mission and the estimated cost of implementation of the recommended option.

1 1 A Changing National Security Landscape

The world that the USAMRIID will operate in over the next two decades will be significantly different from the world just a few years ago. Global changes in society, governments, and technology will all have a major influence on the threats that USAMRIID will face in the future. The convergence of advances in biotechnology and information technology along with the end of the cold war has paradoxically created a world that may be more volatile and dangerous than at any previous period of US history. As we have witnessed, the shift to a wide and unpredictable range of asymmetric global threats has made the US vulnerable to both conventional and non-conventional threats.

During the course of this study, two major terrorist events occurred in the fall of 2001 that had a major impact on the outcome of this plan. The first demonstrated the potential vulnerability of the USAMRIID facility and the need to significantly increase physical security. More directly, the anthrax letters incident in October 2001 thrust USAMRIID directly into the center stage as it rallied to support the nation in responding to the first major bioterrorist event to occur in this country. This event identified new and expanded roles for USAMRIID and also demonstrated vulnerabilities in it capabilities and capacity. The national concern for bioterrorism also resulted in projections of significant expansion in other federal agencies, such as the National Institutes of Health (NIH) which is also initiating major research programs in medical biological defense. These events generated a national consensus to develop a coherent national strategy to include countermeasures to protect the public and the military against biological threats. This mandate will also require the development of a national strategy for biological defense and coordination of efforts with a myriad of federal and state agencies, academic institutions, and industry. This national strategy is expected to significantly expand the number of customers that will require support from USAMRIID.

1.2 Required National Capabilities for Biological Defense

There are several essential capabilities required to develop effective countermeasures against biological threat agents, regardless of whether they are for civilian or military application. First, there must be animal models that simulate human responses in order to evaluate the efficacy of vaccines and drugs under development. Second, the primary route of exposure to threat agents is by inhalation. Therefore, it is essential to evaluate any product being developed for its ability to protect against an aerosol exposure. Third, there must be adequate biocontainment laboratory capacity to support the testing and

evaluation of all the candidate products being developed in animals. Without these capabilities, it will be impossible to conduct the research and development needed to develop products against biological threat agents or to quickly evaluate them. At present, lack of adequate or modern biocontainment laboratory and animal space is the principal physical bottleneck in the research and development pipeline.

1.3 Interagency Relationships

There are several other federal agencies that are playing a growing major role in biological defense research including the Defense Advanced Research Projects Agency (DARPA), the Department of Energy (DOE), Centers for Disease Control (CDC), and the National Institute of Allergy and Infectious Diseases (NIAID). NIAID is one of the organizations that comprise the National Institutes of Health (NIH). It is the lead federal agency responsible for conducting research on infectious diseases. In addition to its intramural research program, NIAID funds a large extramural program through grants to universities and other medical research institutions. NIAID has only recently established a program in bioterrorism research, but it is expected to expand greatly in FY03 with an infusion of ~$1.7 billion[1], with most of the funding to be used for its extramural research program. Based on its Strategic Plan for Bioterrorism, NIAID's program goals complement the USAMRIID research program in several critical areas[2]. For example, NIAID does not have an established biocontainment laboratory infrastructure or a large cadre of experienced scientific personnel to support their bioterrorism research program. In addition, they do not currently own an aerosol testing facility to evaluate their products and would need to contract with USAMRIID or Battelle Memorial Laboratory, the only other facility with a significant aerosol testing capability. Based on the information and products that USAMRIID has already developed, NIAID will be able to significantly accelerate accomplishment of their program objectives. Conversely, USAMRIID would be able to leverage NIAID's vast resources to accelerate the development of products already in the DoD pipeline. There is an opportunity to continue to build on existing scientific and collaborative relationships with NIAID in an effort to leverage the scope of NIAID's bioterrorism program with the distinctive capability inherent in the USAMRIID infrastructure and organization.

[1] Proposed Presidents Budget of the United States, Fiscal Year 2003, Office of Management & Budget, February 4, 2002

[2] The Counter-Bioterrorism Research Agenda of the National Institute of Allergy and Infectious Diseases (NIAID) for CDC Category A Agents, National Institute of Health, February 2002

USAMRIID Mission 2002 – 2015

USAMRIID's organization brings a set of very distinctive capabilities and a 30-year history of research associated with developing medical countermeasures to biological threats. It is the only DoD research entity that possesses aerosol testing facilities for highly pathogenic agents available in the United States that can evaluate animals ranging from rodents to nonhuman primates. It has an experienced Aerobiology Team to study the science of infectious aerosols and aerosolized toxins and develop the technologies required to support testing. USAMRIID also possesses the largest amount of BSL-3 and 4 animal care facilities in the U.S. capable of supporting the testing required for licensure of products for biological threat.

USAMRIID scientists have recently achieved a number of significant accomplishments and milestones. Two vaccine candidates, one for botulinum neurotoxin and the other for Venezuelan equine encephalitis (VEE) virus have recently been transitioned to advanced development. Other products nearing transition include a new recombinant anthrax vaccine, countermeasures for smallpox, and medical diagnostics for infectious disease and biological threat agents. Currently, there are a variety of vaccines for biowarfare (BW) agents in development and USAMRIID has initiated an effort to develop multiagent vaccine(s) that are analogous to commercial combined vaccines such as diphtheria, pertussis, and tetanus (DPT) or measles, mumps, and rubella (MMR). These initiatives will reduce the requirement for the number of stockpiled vaccines and could lead to fewer injections for service members, a simpler vaccination schedule, and a reduced medical logistical burden.

Building on 30 years of vigorous, disciplined, and integrated discovery and development processes, USAMRIID will continue to develop a range of distinctive products and applications critical to the nation's battle against bioterrorism and biowarfare. It is currently recognized as the national leader in biodefense research and is staffed by a knowledge-based workforce of over 650 professional, technical support and administrative staff. The professional staff encompasses a range of scientific disciplines. USAMRIID's strategic focus to mitigate both the intensity and range of traditional and genetically based-engineered threats is through a deliberate process of collaboration with federal and state agencies, industry and renowned academic research institutions. Current organizational efforts are focused on developing team and matrixed units and are aimed at integration of traditional scientific skills with converging disciplines of physics, engineering, information technology, and project management as well as developing the organizational structure that will facilitate adaptation to a dynamic and rapidly changing environment.

In the future, USAMRIID will continue to serve as the lead laboratory for DoD's Medical Biological Defense Research Program (MBDRP). USAMRIID will conduct basic and applied research to develop vaccines, drugs, and diagnostics required to protect the warfighter against biological threats. USAMRIID will also formulate strategies, information, and procedures required to assist the military medical professional in protecting the warfighter. It will serve as the DoD's Level D[3] reference laboratory for definitive diagnostic identification of biological threat agents and the diseases they produce, and will serve as the confirmatory "gold standard" diagnostic reference laboratory. USAMRIID is the DoD's only laboratory for the study of highly hazardous viruses requiring Biological Safety Level 4 (BSL-4) containment[4]. It will support the DoD's Medical Infectious Disease Research Program (MIDRP) in the study of these viruses that are of military relevance and will be the U.S. government's lead laboratory for the definitive testing and evaluation of candidate medical biodefense products for their efficacy in animals.

There are two fundamental differences in the USAMRIID of recent past and the USAMRIID of the future that drive the need for reexamination of the mission and facilities. One is of intensity of research across traditional threat agents as a consequence of the recent use of a biologic agent by a terrorist. The other is a focus toward the development of counter measures against genetically engineered threats, looming anytime between today and the next five years.

1.4 Facilities Infrastructure

USAMRIID is currently housed in nine buildings; four are research or laboratory facilities that provide just over 356,000 gross square feet. One of the two major laboratory facilities is old enough to be designated a National Historic Landmark. The current facility was designed in the late 1950's and built in the early 1960's to accommodate 325 staff. USAMRIID currently has a staff of over 650 personnel.

Based on the results of the strategic and facilities infrastructure analysis, USAMRIID has identified a number of critical capabilities that will be required to support its mission. These include an increased bioinformatics capability, improved and expanded aerobiology facilities, adequately sized animal testing and evaluation facilities, dedicated facilities for Level D confirmatory diagnostics, a small pilot-scale fermentation suite,

[3] Level D laboratory designation is the highest level of confirmatory biological diagnostic capability that possesses the expertise to definitively diagnose an unknown agent.

surge capacity to respond in support of consequence management incidents, and adaptive and modular laboratory facilities at all bio containment levels.

The demand for animals as research models, both rodents and nonhuman primates, has also grown significantly. Rodent populations used in research have grown by 35% between 1998 and 2000. In 2000, there was a demand for approximately 600 nonhuman primates. USRAMRIID only has capacity for 350 at any one time. The demand for aerosol testing has almost doubled from approximately 5000 exposures in the year 2000 to an estimated 8800 exposures for 2002.

There are two scenarios evaluated in master plan study, one is an Addition + Alteration to the existing USAMRIID and the other is a Replacement. These two scenarios meet both existing and projected mission needs of USAMRIID. Under either scenario, USAMRIID needs a facility that is appropriately sized for the larger scope of efforts to develop medical products for eventual licensure. It will execute collaborative, parallel research with a considerably increased staff, more and more modern laboratory space (particularly high containment space), and more resources. The Replacement scenario vastly simplifies the impacts on current and future operations, is less costly, and can be acquired and commissioned in less than half the time.

1.5 Associated Costs & FYDP Scenario

In order to respond to the need for additional and modern laboratory space, increased security, modern and capable animal care needs, and projected consequence management diagnostic capability, the proposed facilities more than triple the current size of USAMRIID from approximately 325,000 square feet to an estimated 1,150,200 total square feet. Construction of replacement laboratory, infrastructure, support, and animal care facilities is estimated to be $826 million with additional supporting costs estimated at $180 million. Table 1 depicts one scenario for FYPD implementation. It does not imply choice of an acquisition or project execution strategy. No funds currently exist in the DoD FYDP or POM for a new, renovated or expanded USAMRIID.

[4] Biological Safety Level 4 (BSL-4) is the highest level of biological containment. Further explanation can be found in Section 2.2 of this report.

	FY03	FY04	FY05	FY06	FY07	TOTALS	Notes:
MILCON	$100	$100	$300	$426		$926	FY03 - $100 Mis for design.
Other Procurement				$2	12.0	$14	Outfitting Costs
Operations & Maintenance			10.0	20.0	$36	$66	Transition costs.
TOTALS	$100	$100	$310	$448	$48	$1,006	

Table 1. Future Years Defense Program implementation schedule. All Figures in $000.

1.6 Conclusion

The Army Surgeon General and USAMRIID have laid the foundation for identifying the requirement for a state-of-the-art, flexible laboratory facility to replace the existing and failing antiquated 30 year-old structure. If funded, design can commence during latter part FY 2002 and be completed by December 2003. Construction could commence in FY 2004. Under this scenario, USAMRIID and its consortium partners could move into the new laboratory in November 2007. In order to accelerate acquisition of the new USAMRIID, it is recommended that an acquisition program office be established that will manage the project and be mandated to employ government and commercial best practices during acquisition.

It is within a very complex and uncertain environment that USAMRIID will operate during the early part of the 21st century. USAMRIID will operate under a new set of assumptions about biological threats for the nation and its warfighters. To be successful, its leaders must have the courage to face the future uncertainty realistically and develop the organizational and physical infrastructure to the meet today's and tomorrow's challenges.

1.7 Navigating the Report

The remainder of the report builds on the Overview discussion. Section 2 describes a very dynamic national security landscape and the external challenges and complexities facing USAMRIID over the next two decades. It further describes critical national biological defense capabilities, existing and proposed relationships between USAMRIID and other federal agencies, and a discussion concerning future USAMRIID customers. Section 3 describes USAMRIID's current and future mission as well as a discussion on current organizational trends to include animal capacity, aerosol testing, and personnel

trending data. Section 4 describes the facility infrastructure requirements and provides a discussion on the operational and infrastructure alternatives considered by the master planning team. Section 5 lays out the projected costs of design, outfitting, construction, and supporting infrastructure for a new USAMRIID. Section 6 describes the proposed costs by fiscal year by category of funds. At section 7 is a conclusion section followed by Appendix A, Frequently Asked Questions and Appendix B, Glossary.

2 Adapting to a Changing National Security Landscape

The world that USAMRIID will operate in 2015 will be significantly different from the world we know today. Global changes in society, governments, and technology will have a major influence on threats that USAMRIID will face in the future. The recent anthrax bioterrorist attack and subsequent consequence management in October 2001 generated national consensus to develop countermeasures to protect the public and the military against biological threats. This will drive the development of a national strategy for biological defense and coordination of efforts with other federal agencies as well as expand the number of customers that USAMRIID will support in the future.

2.1 Global Trends

There are a number of forces that are influencing the future of our national strategy including societal changes, technology convergence, and changes to our national security. Each influences the current and future mission of USAMRIID.

2.1.1 Society and Demographic Changes

By 2015, over half the world's population will be living in megacities, those cities greater than 10 million people[5]. Between 25 to 50% of urban inhabitants in developing countries will live in poverty with potential for tremendous instability, terrorism, and public-health issues. There are also implications for where conflict will occur, the potential for new infectious diseases to emerge, and for bioterrorism and offensive biological warfare to increase. Advancements in information technology are allowing the global community to share information and work cooperatively. USAMRIID is currently engaged in active collaboration with several allied nations on biological defense research. This trend will increase as governments try to leverage each other's R&D programs.

[5] Global Trends 2015: National Intelligence Council, December 2000.

2.1.2 Biotechnology

It is anticipated that there will be major advancements in biotechnology as the various disciplines of biology, physics, and genomics continue to merge with information technologies. Pharmacogenomics will allow for the development of customized and personalized medicine based on genetic profile of individuals. This merger of disciplines will provide new tools and new strategies for developing countermeasures for biological threat agents. It is also anticipated to increase costs and the need for specialized equipment and facilities to conduct research on a range of biological agents.

2.1.3 Pharmaceutical Industry

The average cost of developing a new drug is $500 million and takes 10–15 years. Only one out of 10 potential new drugs in transition from Discovery Research to Phase I clinical safety trials ultimately achieve FDA licensure[6]. R&D costs are 15%-20% of all pharmaceutical sales. The pharmaceutical industry faces some very significant challenges, such as harnessing biotechnology, controlling R&D costs, streamlining the development cycle, shortening the FDA approval process and enduring in the potential implications of customized medicines that may undermine the capabilities of producing "blockbuster" drugs. As a consequence, there is the potential for greater interest from the industry to assist the government in developing vaccines, drugs, and diagnostics for biological threats. Such industry support will be critical for transitioning candidate products developed at biodefense research institutions, such as USAMRIID, into licensed products.

2.1.4 The Threat

Revelations about the scale of the former Soviet offensive biowarfare program during the past decade suggested that the Soviets program was designed to be effective if used against large population centers. Although the Soviet and US programs were dismantled, smaller rogue nations, such as Iraq, view the development of biological weapons as a cheap way of acquiring weapons of mass destruction and geopolitical power. Although many countries have the ability to produce large quantities of these biological agents, their use as weapons of mass destruction require the development of sophisticated delivery systems, such as ICBMs, that are not easily duplicated by smaller nations and terrorist groups. Although the likelihood is low that such weapons of mass destruction will ever be used, the number of resulting casualties could be potentially enormous. More probable is the use of biological weapons by terrorist groups to achieve political goals. Groups such as Aum Shinrikio and Osama Bin Laden's al

6 Why Prescription Drugs Cost So Much, The Pharmaceutical Research and Manufacturers of America (PhRMA), June 2000.

Qaeda network have already attempted to develop biological weapons. These threat agents are easily obtained from nature or other sources and can be grown. In addition, the recent anthrax letters incident demonstrated how easy it is to cause fear and disruption of our society, which will encourage even more groups to use bioterrorism as a means to achieve political objectives.

To date, the primary focus of USAMRIID has been on developing countermeasures for the classical biological threat agents used in warfare such as anthrax and smallpox. However, there is evidence to suggest that future threats could be based on genetically modified organisms. For example, the former Soviet program developed genetically modified versions of the classical threat agents that were resistant to multiple antibiotics or that expressed bioregulator molecules capable of disrupting the regulatory systems of the body. Advancements in biotechnology allow almost anyone with the proper knowledge, reagents, and equipment to genetically modify microorganisms to possess new traits that potentially could be more lethal or that circumvent our ability to protect against a known threat agent. These risks will pose new challenges for developing defensive countermeasures to protect the nation and its warfighters against these threats.

2.2 Levels of Biocontainment

Given the implications of acquiring a new facility to support the USAMRIID mission, it is important to understand the characteristics of various levels of biocontainment and their implications on scope and eventual cost. What follows is a short discussion on biocontainment. Biological laboratories are categorized into four levels:

- **Biosafety Level 1 (BSL-1)** is suitable for work involving well-characterized agents not known to consistently cause disease in healthy adult humans, and of minimal potential hazard to laboratory personnel and the environment. The laboratory is not necessarily separated from the general traffic patterns in the building. Work is generally conducted on open bench tops using standard microbiological practices. Special containment equipment or special facility design is neither required nor generally used. Laboratory personnel have specific training in the procedures conducted in the laboratory and are supervised by a scientist with general training in microbiology or a related science.

- **Biosafety Level 2 (BSL-2)** is similar to Biosafety Level 1 and is suitable for work involving agents of moderate potential hazard to personnel and the environment.

It differs from BSL-1 in that (1) laboratory personnel have specific training in handling pathogenic agents and are directed by competent scientists; (2) access to the laboratory is limited when work is being conducted; (3) extreme precautions are taken with contaminated sharp items; and (4) certain procedures in which infectious aerosols or splashes may be created are conducted in biological safety cabinets or other physical containment equipment.

Biosafety Level 3 (BSL-3) is applicable to clinical, diagnostic, teaching, research, or production facilities in which work is done with indigenous or exotic agents which may cause serious or potentially lethal disease as a result of exposure via inhalation. Laboratory personnel have specific training in handling pathogenic and potentially lethal agents, and are supervised by competent scientists who are experienced in working with these agents. In a BSL-3 environment, all procedures involving the manipulation of infectious materials are conducted within biological safety cabinets or other physical containment devices, or by personnel wearing appropriate personal protective clothing and equipment. The laboratory also has very specialized engineering and design features.

- **Biosafety Level 4 (BSL-4)** is required for work with dangerous and exotic agents that pose a high individual risk of aerosol-transmitted laboratory infections and life-threatening disease. Agents with a close or identical antigenic relationship to Biosafety Level 4 agents are handled at this level until sufficient data are obtained either to confirm continued work at this level, or to work with the agents at a lower BSL level. The laboratory staff has specific and thorough training in handling extremely hazardous infectious agents and understands the primary and secondary containment functions of standard and special practices, the containment equipment, and the laboratory design characteristics. The staff is supervised by competent scientists who are trained and experienced in working with these agents. The laboratory director strictly controls access to the laboratory. The facility is either in a separate building or in a controlled area within a building, which is completely isolated from all other areas of the building. A specific facility operations manual is also prepared or adopted. Within work areas of the facility, all activities are confined to Class III biological safety cabinets, or Class II biological safety cabinets used with one-piece positive pressure personnel suits ventilated by a life support system[7]. The Biosafety

[7] The biological safety cabinet (BSC) is the principal device used to provide containment of infectious splashes or aerosols generated by many microbiological procedures. There are three types of biological safety cabinets (Class I, II, III) used in microbiological laboratories, open-fronted Class I and Class II biological safety cabinets are primary barriers, and gas-tight Class III biological safety

Level 4 laboratory has special engineering and design features to prevent microorganisms from being disseminated into the environment.

Containment is the critical issue associated with research involving biological agents. Until the time that a sample is categorized it must be handled as the highest level of potential threat - highly infectious and lethal. Due to the hazardous nature of the agents handled in laboratories with designations higher than BSL-2, it is not unusual for there to be community concerns about the presence of such laboratories. There are several examples of BSL-4 laboratories being constructed, but never opened or operated at the BSL-4 level due to community, environmental, management, sustainment and operational concerns.

2.3 Biodefense National Strategy - The Military & Civilian Interface

The traditional cornerstone of military medical doctrine has been to conserve fighting strength of the warfighter. Consistent with that doctrine, the emphasis of the DoD Medical Biological Defense Research Program (MBDRP) has been to develop prophylactic countermeasures, such as vaccines, against the classical biological threats,

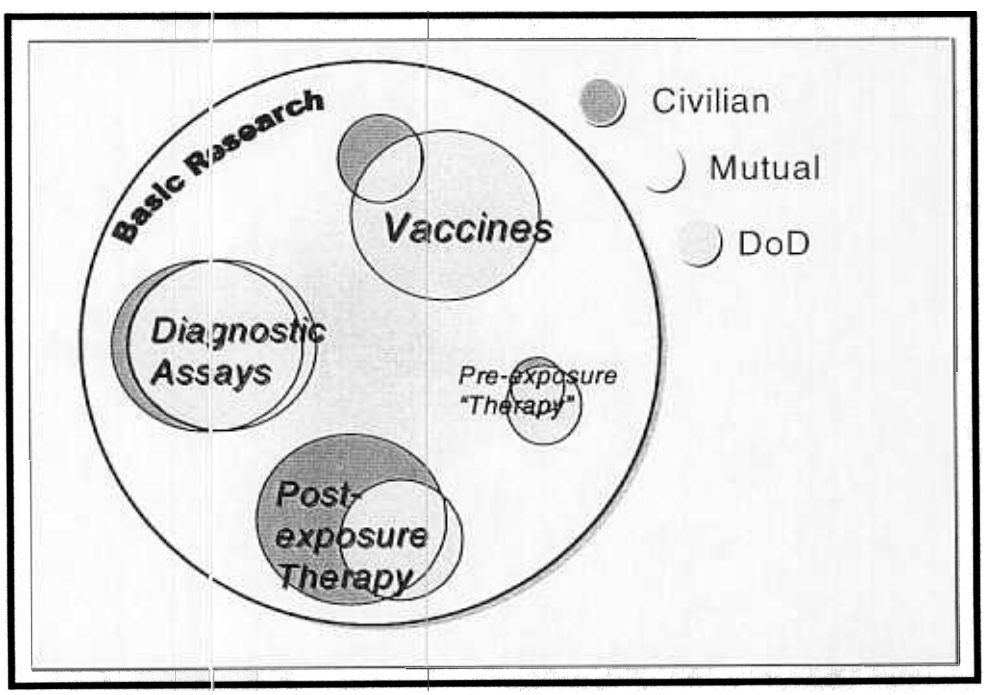


Figure 1. Relationship of varying biomedical research components across DoD and civilian sectors

cabinets provides the highest attainable level of protection to personnel and the environment. Extracted from the CDC / NIH Biosafety in the Microbiological and Biomedical Laboratories, 3rd Edition, March 1993.

since vaccines afford better protection and require less supportive care than therapeutics given after exposure. This approach results in soldiers, sailors, airmen and marines that are healthy and able to fight in an uninterrupted manner. To be effective, these vaccines would have to be given to the warfighter prior to deployment to the theater of war. Such a strategy is possible if the size of the population is sufficiently small and well controlled with regard to age and health status, and compliance can be made mandatory. However, for most agents, this approach will not likely be used for protecting the entire civilian population since the cost would be prohibitive. There would also be significant personal liberty and legal impediments to achieving compliance with a mandatory vaccination program. It is more likely that post-exposure treatment will be the preferred method of protecting the public. Figures 1 and 2 graphically describe these differences.

To protect both civilian and military populations against genetically engineered threats that may be encountered in the future, emphasis will have to be placed on developing novel, broad-spectrum therapies. This strategy is key since development of specific countermeasures against each threat is and will continue to be a great scientific and medical challenge. Defense against these threats will depend on the use of bioinformatics to scan genomic and proteomic databases to identify common motifs that are shared by the threat organisms and then rationally design therapeutic countermeasures that disrupt them while not affecting the host. This will be a major challenge and can only be solved by research and use of the latest tools of biotechnology.

2.4 Required National Capabilities for Biological Defense

There are several essential capabilities required in order to develop effective countermeasures against biological threat agents, regardless of whether they are for civilian or military application.

First, it is important to have animal models that duplicate, as closely as possible, the human disease. Most of these biological agents do not normally infect man and cannot be effectively or scientifically studied or controlled. Without these models, it would be impossible to evaluate the efficacy of vaccines and drugs under development.

Second, the primary route of exposure to these threat agents is by inhalation. It is essential to evaluate any product being developed for its ability to protect against an aerosol exposure.

- Third, there must be adequate biocontainment laboratory capacity to support the testing and evaluation of all the candidate products being developed in animals.

Without these capabilities, it will be impossible to conduct the R&D required to develop products against these biological threat agents and to evaluate them quickly. At present, biocontainment laboratory space is the principal bottleneck in the basic and advanced R&D pipeline in both the DoD and at the National level.

Other Federal Agencies: Roles and Capabilities

There are several other federal agencies that are assuming a new or larger role in biological defense research. A key point to consider is that only CDC has any appreciable amount of biocontainment laboratory infrastructure that is essential for accomplishing basic and advanced R&D required to protect both civilian and military populations.

Defense Advanced Projects Agency (DARPA)

DARPA, an agency of the Department of Defense (DoD), funds two programs that are focused on supporting research on biological threat agents. This work is accomplished extramurally through grants and contracts to universities and other institutions. DARPA research that shows promise is transitioned to the core Medical Biological Defense Research Program (MBDRP) for further testing and evaluation by USAMRIID. DARPA has funded the construction of a BSL-3 small animal testing facility at the University of New Mexico to support evaluation of its concepts. The University of New Mexico does not have a BSL-4 facility.

Department of Energy (DOE)

The DOE, through its Chemical and Biological Nonproliferation Program (CBNP), conducts research on biological threat agents. Due to its strengths in computer modeling and simulation of nuclear weapons, the focus of the CBNP has been on modeling how the release of a biological agent would disseminate through a city, building, or subway, and how to harden such facilities against a biological attack. In addition, the CBNP studies the genomic of microbial pathogens in order to develop microbial signatures that could be used to detect them in the event of a release. The CBNP does not work directly on developing medical countermeasures and currently only possesses a small BSL-3 biocontainment laboratory. It has no BSL4 facility.

2.5.3 Centers for Disease Control (CDC)

The CDC is the federal agency primarily responsible for protecting the public health. It is the lead agency for formulating plans and responding to a domestic bioterrorism event. The CDC is designated a Level D laboratory (highest) in the Bioterrorism Preparedness and Response Network. It is the only laboratory, other than USAMRIID, that has the biocontainment laboratories and expertise to definitively diagnose an unknown agent. The CDC's strengths are in the epidemiology, diagnosis, and response to a disease outbreak. The CDC works in close collaboration with USAMRIID to develop diagnostic systems that can detect biological threat agents. It also has responsibility for establishing pre-positioned stockpiles of drugs and vaccines to protect the public in the event of a bioterrorism incident. Although the CDC conducts some basic research on biological threat agents, it is not CDC's primary mission. The CDC is currently expanding its BSL3 and 4 biocontainment laboratories at its campus in Atlanta. This will bring the CDC to 13,800 NSF of BSL 3 and 13,800 NSF of BSL 4 laboratory space. These laboratories will be used primarily to develop diagnostic assays and to handle, identify, and characterize unknown disease-causing agents. The CDC is currently the only other federal agency that has any significant biocontainment laboratory infrastructure.

2.5.4 National Institute of Allergy and Infectious Diseases (NIAID)

NIAID is one of the organizations that comprise the National Institutes of Health (NIH) and is the lead federal agency responsible for conducting research on infectious diseases. In addition to its intramural research program, NIAID funds large extramural programs through grants to universities and other medical research institutions. Based on its Strategic Plan for Bioterrorism, NIAID's program goals compliment the USAMRIID research program. Although the scale of NIAID's intra and extramural programs will be very large compared to the USAMRIID mission, there are critical areas where USAMRIID complements NIAID. A proposed collaborative partnership, showing the relative strengths of each organization and their potential roles, is depicted in Figure 3.

NIAID currently only has a modest amount BSL-3 laboratory space. However, it intends to expand this capacity by:

1. Expanding its BSL-3 laboratory on the NIH Campus in Bethesda, MD
2. Building a BSL-4 lab in Hamilton, MT
3. Building a BSL-4 patient isolation unit at Fort Detrick, and
4. Building ten regional BSL-3 containment laboratories to support its extramural program.

These ten regional centers will reduce some of the demand for BSL-3 biocontainment laboratory space, especially for university researchers. However, these facilities are not

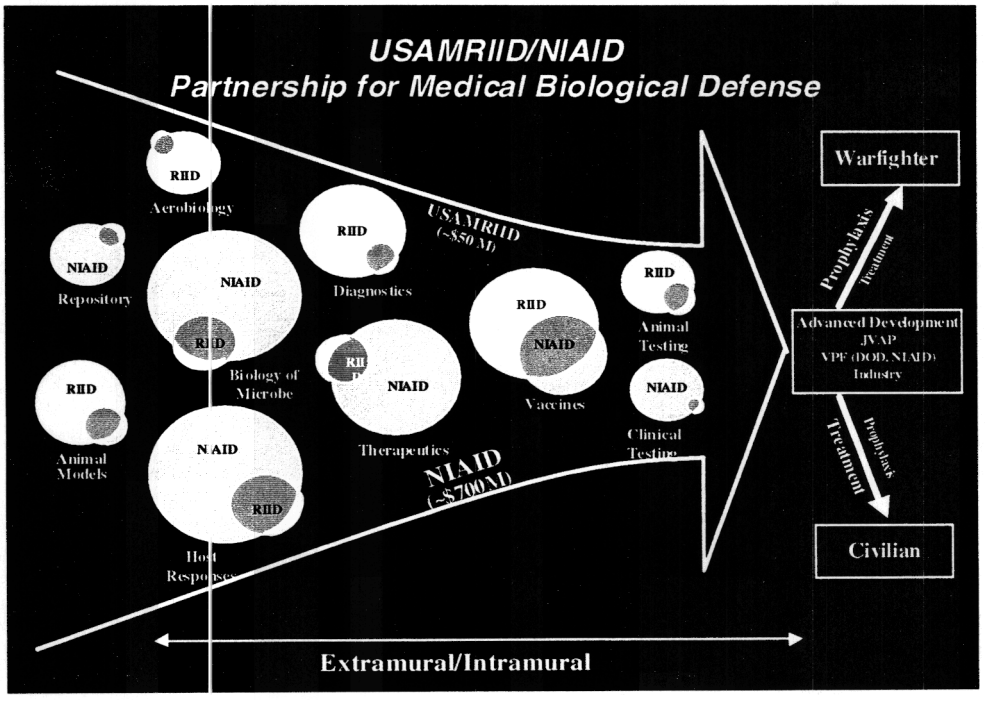


Figure 3. Proposed USAMRIID/NIAID Biological Defense Partnership

currently anticipated to be able to conduct the pivotal aerosol challenge studies using large groups of animals required to support advanced development and FDA licensure. The Deputy Assistant to the Secretary of Defense (DASD) for Chemical and Biological Defense (CBD) has encouraged USAMRIID to coordinate its research program with NIAID and collaborate to the fullest extent possible. A stronger and well-coordinated relationship between USAMRIID and NIAID can leverage each organization's respective strengths and would mutually benefit both programs. In addition, coordination of the two programs would minimize duplication of effort, resources, offer the opportunity to share support and animal facilities, and ensure that solutions needed to protect both the civilian population and the warfighter against biological threat agents are developed as efficiently as possible.

2.6 Anticipated USAMRIID Customers

Based on the trends USAMRIID has observed during the past several years, some key assumptions were made in defining the future role of USAMRIID and its customers.

These assumptions are critical in defining the mission of USAMRIID for the future and ensuring that there is adequate infrastructure to support projected needs.

2.6.1 DoD

The primary assumption is that USAMRIID will continue to serve as the lead laboratory for the DoD's Medical Biological Defense Research Program (MBDRP) and will continue to focus on conducting R&D to support the warfighter's unique needs, with research primarily focused on developing vaccines and diagnostics. USAMRIID will continue to support the DoD's need for definitive identification of unknown biological agents by serving as the DoD's Level D reference laboratory and will continue to conduct research of highly hazardous viruses requiring BSL-4 containment as part of the DoD's Medical Infectious Disease Research Program (MIDRP).

2.6.2 NIAID

The primary emphasis of the NIAID bioterrorism research program will be on basic research on threat agents and development of therapies to protect the public. NIAID does stipulate the development of new vaccines in its strategic plan. It is anticipated that USAMRIID will play a key role in the NIAID program. They will use USAMRIID's facilities, capabilities, and expertise to test and evaluate candidate products being developed through their program.

2.6.3 United States Department of Agriculture (USDA)

Medical research that impacts all populations will continue to grow as more information is found and shared in the emerging study of agriculture related threats. The outbreak of Foot and Mouth Disease in England demonstrated the economic impact associated with animal diseases. A variety of other diseases with potentially devastating agricultural economic losses are being considered form the perspective of bioterrorism. Some of these agents also affect humans. In the past few years USAMRIID has assisted in research associated with mosquito-borne disease, such as the outbreak of West Nile virus in the human and bird population of the Northeastern United States. Such diseases constitute another biological threat to the interest of the nation. It is anticipated that the USDA, as well as state agricultural agencies, will turn to USAMRIID for assistance in the identification and study of such diseases especially by aerosol dissemination.

2.6.4 Others

Many other interested groups have approached USAMRIID for access to its biocontainment laboratories. These customers range from other government agencies (FDA, DARPA, FBI, Secret Service, Capitol Police, and DOE), to universities and

biotechnology companies. During the past several years there has been an increased demand for USAMRIID to conduct aerosol studies in animals in support of the candidate products produced by these groups. USAMRIID currently has more demand than it can accommodate. The general increase in funding for bioterrorism research is expected to increase demand even further, thereby exacerbating the bottleneck in getting candidate products evaluated. USAMRIID has also been requested occasionally to assist foreign governments in identifying outbreaks of unknown diseases.

3 USAMRIID's Current & Future Mission (2002 - 2015)

USAMRIID is expected to undergo a major evolution during the next decade. This evolution will affect the entire organization and will include its mission, research goals, required personnel, organizational structure, and infrastructure needs. Some of the infrastructure required to support USAMRIID's mission in 2015 is already known, since these deficiencies already exist today. Other requirements are based on a range of plausible future scenarios.

3.1 Current Mission

The current mission statement of USAMRIID is as follows:

> *Conduct research that leads to medical countermeasures including vaccines, therapies, diagnostics, and information to protect U.S. military personnel against biological threat agents*

USAMRIID's primarily mission is to support the warfighter's requirements for medical biological defense. It is a "tech-base" organization, where vaccines, diagnostics, and therapeutics are discovered, refined, and taken through various stages of testing in animals before hand-off to an advanced developer for production and testing in humans. USAMRIID does not possess the manufacturing facilities and expertise required to produce pharmaceutical products. It is dependent on other entities to carry its candidate products through advanced development.

3.2 On-Going Work

Consistent with this mission, USAMRIID has been working on a number of products over the past several years. Two vaccine candidates, one for botulinum neurotoxin and the other for Venezuelan equine encephalitis (VEE) virus have recently been transitioned to advanced development. Other products nearing transition include a new recombinant anthrax vaccine; countermeasures for smallpox; and medical diagnostics for infectious disease and biological threat agents. There are several other products for protection

against biological threats in the USAMRIID discovery pipeline that appear promising and that should be ready for transition to advanced development with the next several years.

Currently, the Department of Defense has identified a need for over a dozen vaccines against biowarfare (BW) agents. Many of these are in various stages of development. USAMRIID has also initiated an effort to develop multiagent vaccine(s) that are analogous to commercial combined vaccines such as diphtheria, pertussis, and tetanus (DPT) or measles, mumps, and rubella (MMR). This effort would reduce the requirement for the number of stockpiled vaccines and could lead to fewer injections for service members, a simpler vaccination schedule, and a reduced medical logistical burden.

In addition to vaccines and therapeutics, the institute develops diagnostic assays for biological threat agents and infectious diseases. The ability to diagnose infection immediately after exposure is critical to determining appropriate treatments and may be important in establishing proof of biological weapons use. Over 50 assays have been developed and optimized to date for 26 different biological threats that may confront our warfighters. Information gained through USAMRIID's response to bioterrorism is transferred to an emerging DoD laboratory response network. Techniques and methods compatible with the CDC National Laboratory Response Network have been shared with over 33 military laboratories through videotapes and CD-ROM disks. These activities contribute directly to an improved response and readiness to biological threats at Army and DoD medical centers.

3.3 Future Mission

The future mission of USAMRIID has been defined based on consideration of future threats and the roles of other federal agencies in supporting work on medical biological defense. The key element that differentiates USAMRIID from any other federal laboratory is its focus on providing biological defense products to our nation's warfighters. However, national requirements are expected to drive the need for a federal consortium to address this problem. The unique capabilities required to develop solutions for the warfighter will have direct applicability for support of the public as well. Thus, USAMRIID is expected to play a critical role in the future as a member of this consortium in developing products and strategies required to protect the public.

> USAMRIID will serve as the lead laboratory for DoD's Medical Biological Defense Research Program (MBDRP). USAMRIID will conduct basic and applied research to develop vaccines, drugs, and diagnostics required to protect the

warfighter against biological threats in the field. USAMRIID will also formulate strategies, information, and procedures required to assist military medical professional in protecting the warfighter.

USAMRIID will serve as the **DoD's Level D reference laboratory** for definitive "gold standard' diagnostic identification of biological threat agents and the diseases they produce. In addition, USAMRIID will serve as the confirmatory diagnostic laboratory for the National Capitol Area (NCA).

USAMRIID will serve as the DoD's only laboratory for the **study of highly hazardous viruses requiring BSL-4 containment**. It will support the DoD's Medical Infectious Disease Research Program (**MIDRP**) in the study of these viruses that are of military relevance.

USAMRIID will serve as the U.S. government's lead laboratory for the **definitive testing and evaluation of candidate medical biodefense products for their efficacy in animals**.

3.4 Current Organizational and Mission Trends

3.4.1 Animal Usage

USAMRIID has one of the finest animal research programs in the DoD. It is held in high regard by the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC). With several thousand animals across a range of species, the program provides significant benefit to test and evaluation of medical products for protection of the warfighter, as well as the civilian and potentially domestic animal populations. Figure 4 depicts the trend in rodent testing at USAMRIID. In general, the demand for animal testing has continued to increase over time. Figure 5 depicts the census of nonhuman primates at USAMRIID during the past several years. Demand significantly increased in FY00 and continues today at extremely high levels. The current facility, however, does not have sufficient capacity to house more than ~350 primates at any given time. This has placed a major constraint on the usage of primates. Additionally, rooms used for housing primates cannot be used for maintaining other larger animal species, like rabbits. This has placed constraints on the number of rabbit studies that can be performed concurrently. Funds totaling approximately $600,000 will be spent in FY 02 to house animals at distant facilities, requiring higher per diem charges and increased logistics, transportation and security than would be required if the population was housed at USAMRIID.

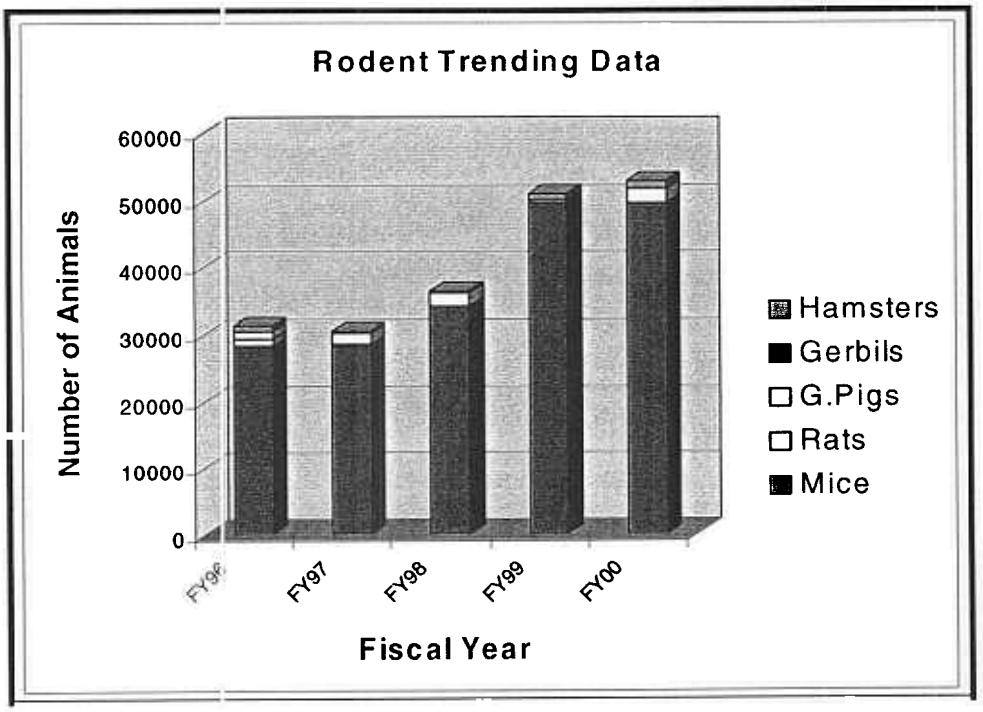


Figure 4. USAMRIID rodent trends by year

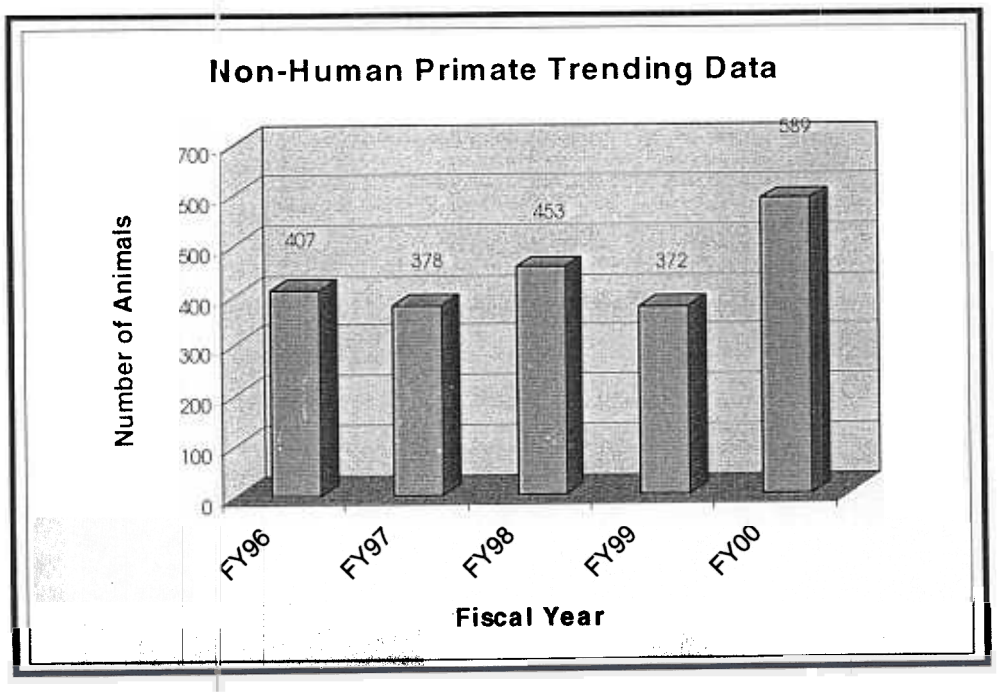


Figure 5. Census of nonhuman primates at USAMRIID by year

3.4.2 Aerosol Testing

Figure 6 depicts the trend in aerosol testing of animals at USAMRIID. As the graph indicates, the demand for aerosol testing has exponentially increased over the past several years. Current FY02 numbers suggest that this trend will continue for the foreseeable future.

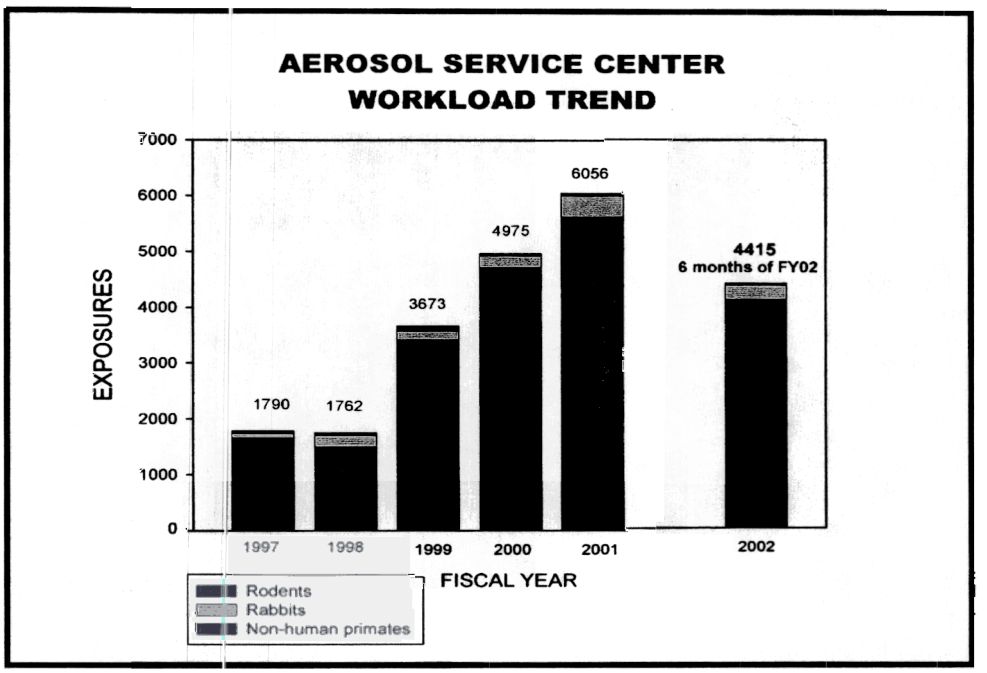


Figure 6. Aerosol Workload Trends

3.4.3 Facility Repair and Maintenance Costs

Figure 7 depicts repair and maintenance costs that have continued to escalate exponentially as a function of the total institute budget. This is due to the age of the primary biocontainment facilities. Building 1425 exceeds 30 years and mechanical, electrical, and HVAC systems are failing. The other facility, building 1412, is 45 years old and presents even greater challenges to maintain. The fluctuations shown in the graph can be attributed to years where there were major cost equipment failures, such as chillers used for air conditioning, that were replaced. This trend is alarming, since the total institute budget has not increased significantly since FY1995. If this trend continues, there is great risk that a significant portion of USAMRIID's budget will be dedicated to repair and maintenance of the facility in order to keep it operational. This would have an adverse effect on the ability of the core research program to accomplish its goal.

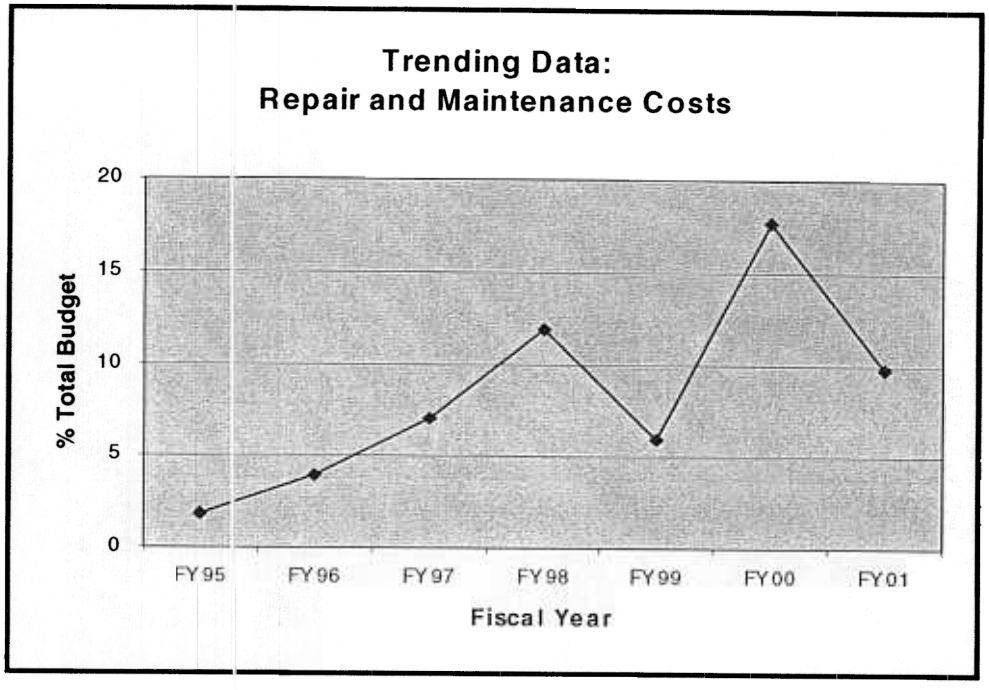


Figure 7. Repair and Maintenance Trend Data

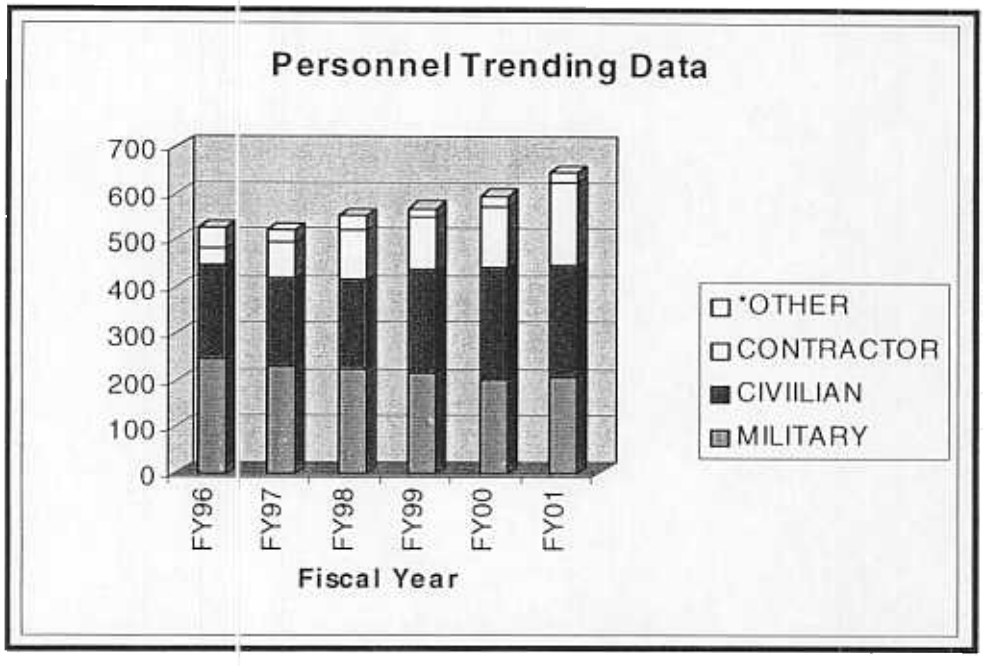


Figure 8. USAMRIID personnel trend data by year

Personnel

The current facility infrastructure was originally designed to house ~325 staff. Over the past decades, there has been significant growth in the DoD's Medical Biological Defense Research Program (MBDRP), particularly since the Gulf War in 1989. This has resulted in a concomitant growth in the number of personnel required to conduct research and to support increased demand for testing. Figure 8 depicts the trend in personnel growth over the past six years depicting the current staff of ~650 personnel.

Distinctive Capabilities

USAMRIID currently possesses several unique capabilities that support its efforts in biological defense research. These capabilities include:

The greatest amount of containment laboratory space in the United States (currently).

- 6,700 net square feet of BSL4 space (the highest level of containment)
- 40,500 net square feet of BSL3 space
- 200,000 net square feet of BSL2 space

- The only high containment facilities designed for clinical studies of BSL-3 level materials and for the treatment of human subjects accidentally exposed to virulent organisms.

  BSL2 and BSL3 Clinical Diagnostic Facility and Ward (16 beds)
  BSL4 Patient Isolation Facility (only other such facility is in Novosibirsk, Russia)

- The only Aeromedical Isolation Team (AIT) that can transport patients safely back to USAMRIID for care and treatment

  The only Level D Diagnostic Reference Laboratory in the DoD and one of two in the entire U.S. (CDC being the other)

- The only DoD aerosol testing facilities for highly pathogenic agents that can evaluate animals ranging from rodents to nonhuman primates.

  Unique Aerobiology Team to study the science of infectious aerosols and to develop the technology required to support testing.

The only BSL3 level medical entomology suite in the U.S. capable of performing vector competency studies with a wide variety of viral pathogens.

Capability to perform cGLP (Current Good Laboratory Practices) studies under containment conditions.

Board-Certified Veterinary Pathologists and facilities for conducting autopsies under biocontainment

Lab Animal Veterinarians experienced in the care and handling of infected animals (rodents, lagomorphs, non-human primates)

- The largest amount of BSL-3 and 4 animal holding facilities in the U.S. capable of supporting the testing required for licensure of products for biological threat.

  Extensive collection of strains, hybridomas, genes, and other reagents

  Related infrastructure (waste management, safety, security, etc.) required to support the laboratory.

3.5 Future Requirements

Future requirements are a function of lessons learned over the past decade as well as fundamental changes as a consequence of the anthrax letters incident, advanced development challenges as well as capacity challenges associated with aerosol testing and animal facilities, and new organizational capabilities.

3.5.1 Past Outbreaks

Based on past events, there have been several lessons learned and capabilities required that must be considered when determining USAMRIID's infrastructure requirements. In general, whenever there has been a biological incident, USAMRIID has been called upon to assist. For example, in past outbreaks, USAMRIID has sent teams out to the field to collect samples and bring them back to the laboratory to identify unknown agents. The West Nile virus outbreak in New York City in 1998 is a more recent example of when USAMRIID has been called upon to assist and to identify the unknown agents. In 1989, nonhuman primates located at a private animal holding facility in Reston, VA began to die suddenly. USAMRIID scientists were called upon to identify the cause of death of these animals. It was determined that these monkeys were infected with Ebola virus. USAMRIID scientists, working in close collaboration with

the CDC, were called upon to eradicate the outbreak in the primate facility and to decontaminate the building to ensure that the virus did not spread to the local population. These efforts required a field-deployable team of experts to collect samples, identify the unknown agent rapidly, and then assist in eradicating the infection and decontaminating the building. USAMRIID must have the dedicated infrastructure required to support these field-deployable teams and to transport and hold patients that may be infected with an unknown agent.

3.5.2 Anthrax Letters Incident

On October 15, 2001, an employee in Senator Thomas A Daschle's office opened a letter that contained powdered anthrax. Within hours the FBI delivered the letter and its remaining contents to USAMRIID, which analyzed the material and determined it to be a surprisingly virulent strain of anthrax. In the months that followed, USAMRIID became the focal point for testing these samples. Prior to October 2001, USAMRIID was normally handling about ten samples a month, sent by the FBI or Secret Service. This was accomplished with a staff of six in the Special Pathogens Sample Test Laboratory. By the end of October, the staff grew to 82 personnel, drawn from other elements of the USAMRIID staff and from other military medical units. Working 24 hours a day with three shifts, USAMRIID was able by the end of October to process 100 samples a shift. In November 2001, another letter to Senator Patrick Leahy was discovered and immediately delivered to USAMRIID for testing and evaluation. By April 2002, the lab processed nearly 25,000 samples and performed more than 200,000 specialized tests to determine the content of the samples. This effort placed an enormous load on USAMRIID and required it to reallocate space and personnel in part because it did not have the proper infrastructure required to support the effort. This event emphasized the need for USAMRIID to have a dedicated diagnostic laboratory infrastructure of sufficient capacity to support an event of this magnitude in the future.

3.5.3 Animal Capacity Challenges

It has become clear that there are insufficient commercial biocontainment facilities available to support the aerosol challenge studies in animals required by the Advanced Developer to support FDA licensure of their products. Therefore, USAMRIID will need to have a sufficient number of adequately sized animal rooms and staff to support the Advanced Developer's needs, regardless of whether it is a government or commercial entity. This capability will be essential for providing the pivotal data required to support licensure, since the FDA will require extensive animal testing to prove the efficacy of a product in the absence of human clinical testing.

3.5.4 New Critical Capabilities

Based on a series of strategic planning exercises held during the past 12 months, USAMRIID has identified several capabilities that will be required to support its mission in over the next two decades. These include the following:

Greater emphasis on the development of broad-spectrum therapeutics for genetically modified organisms

Possibility that future vaccines and therapies will have to be custom-tailored for each individual

A strong bioinformatics capability

Improved and expanded aerobiology facilities

Dedicated animal testing and evaluation facilities

- Dedicated facilities for the Level D confirmatory diagnostics mission
- A small pilot-scale fermentation suite
- A BSL-4 patient isolation unit
- A dedicated secure central repository for storage of biological threat agents

Field-deployable investigative teams and transport isolator capability

Excess surge capacity to respond to incidents

Adaptive and modular biocontainment laboratory facilities

Office and meeting rooms designed to facilitate multidisciplinary teaming and communication

4 Infrastructure

4.1 Current State

USAMRIID is currently housed in nine buildings; four are research laboratory buildings, which provide just over 356,000 gross square feet. One of the two major laboratory facilities is has been designated a National Historic Landmark. The main research building (Bldg 1425) was constructed in 1970, over 30 years ago. One of the other permanent research buildings was constructed in 1956 and another was constructed in 1958. The newest research building was constructed in 1986; however, it is temporary construction. The main research building (Bldg. 1425) houses all BSL 4 laboratories

(the highest containment level for the most dangerous of infectious diseases) and most of the BSL 3 to BSL 1 laboratories. USAMRIID currently houses the largest BSL 4 facility in the United States.

By the nature of the work with highly infectious, often lethal organisms and toxins, the facility requirements are very specialized, requiring high degrees of sophistication for biological safety of the occupants, biological containment of the agents, and biological security of the premises. The existing containment laboratories at USAMRIID are based on concept of design and technology of the 1960s. Likewise the mechanical, electrical, ventilation, and alarms systems are old and increasingly less serviceable. Regulatory standards in the areas of animal housing, good laboratory practices, and healthcare facilities have changed since the late 1960s. All of these changes require more space to meet today's standards. While the basic concept of biocontainment has changed little, the technology and material that assures containment have progressed. Significantly better air handlers, filters, finishes, monitors and seals are now available.

Even prior to the anthrax bioterrorism attack in the fall of 2001, USAMRIID was struggling to meet its mission within the current facilities. An effort to develop a facilities upgrade and recapitalization plan for USAMRIID was begun in September 2000. The surge in research, development and diagnosis after the anthrax letters incident further demonstrated the inadequacies of the existing facilities and the need to refine the execution of a master plan to provide modern, appropriately sized laboratory facilities.

USAMRIID's facility shortcomings fall largely into two categories: space and age. Studies in 1985, and again in 1986, by the firms of Colimore/Clark Associates and Ross, Murphy, Finkelstein, Inc., found that USAMRIID needed more space to accomplish its biological defense research mission. The 1986 study included a finding that:

> *"There is insufficient space to adequately house even the current compliment of personnel, research and support activities. There is no space to accommodate recent mission enhancements and expansions."*
>
> *Ross et al 1986*

Since these studies, the USAMRIID staff has grown by 65 percent, with no addition to the research space. This has been accomplished through reduction in the amount of space allocated to individuals for office and laboratory use, use of temporary building space, and conversion of hallways in several instances as extended office space for post-doctoral fellows. A 2002 study conducted by SRA International, Inc. and CUH2A (High Containment and Laboratory architects) shows that when benchmarked against

any other similar laboratory facility, USAMRIID is found to have the least laboratory space per researcher and the oldest containment facilities.

The existing laboratory buildings do not take advantage of the advances in air handing, computerized control systems, surveillance, heating/cooling, installed research equipment, or biological containment. The layout of the laboratories creates inefficiencies and hampers the work efforts. Modern concepts for laboratory design associate BSL 4 laboratories with BSL 3 laboratories to allow the researchers to "step down" from higher containment areas and keep working, without having to enter and exit the various containment areas. Research demands and limited containment space have forced researchers to share laboratory space. This creates safety problems as well as efficiency concerns. Because they are working in laboratory spaces where multiple agents are present, researchers that are studying only one threat agent must be vaccinated and tested against numerous agents,

Current major facility issues requiring attention include:

Additional biological containment laboratories for research

- Specialized laboratory space for aerobiology
- Additional biocontainment animal facilities

Additional office/support space to alleviate overcrowded conditions and to expand research efforts

- Renovation of existing laboratories to incorporate state-of-the-art biocontainment technology

Renovation of existing mechanical and electrical systems

Force protection, operational redundancy, and biological security upgrades.

4.2 Proposed Facilities

In early 2001, USAMRIID initiated a study to document its facility requirements and create a master plan. This effort was undertaken under the supervision of the Army Surgeon General. The contract team of SRA, International, Inc. and the architectural firm CUH2A undertook this work. The projections of USAMRIID facility requirements are based on the application of current standards of practice for: medical research, laboratory animals, healthcare organizations, and biohazard containment and security. Where comparisons exist, the needs of USAMRIID were benchmarked against such

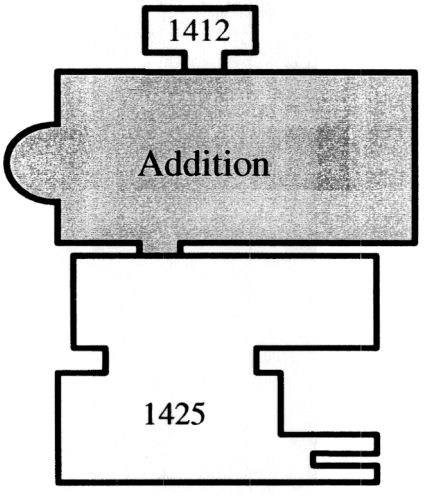
facilities as the CDC. This study reviewed two alternative facility solutions. The results of the study are summarized below.

There are two scenarios considered in this study. One is an Addition + Alteration and the other is a Replacement. These two scenarios are facility solutions to both existing and new mission needs of USAMRIID. Under either scenario, USAMRIID is a facility that is more appropriately sized for the larger scope of efforts to make medical products for eventual licensure. It will execute collaborative, parallel research with a considerably increased staff, more laboratory space, and more resources. The facility scenarios both will house the same projected growth in laboratory animals, investigators, supporting staff and other resources. In fact, each would provide 108,225 NSF of BSL 2, 86,525 NSF of BSL 3, and 38,393 NSF of BSL 4 laboratory space. A discussion of the alternatives and the operational impact resultant from the two facility scenarios follows.

4.2.1 Addition + Alteration

The addition + alteration is the more complex of the scenarios and has the greatest impact on the operations of USAMRIID for the longest period of time. This is also the more costly scenario. The existing relationship of the two dominant buildings operated by USAMRIID is shown in the graphic Addition + Alteration-1 and these proceeds through 4 distinct phases depicted on the subsequent charts. The first phase of the construction would be to construct an addition in the area between building 1412 and 1425. This addition would decompress a portion of the existing USAMRIID operational elements and these elements would vacate their existing administrative and laboratory space to move into the addition.

Addition+Alteration-1

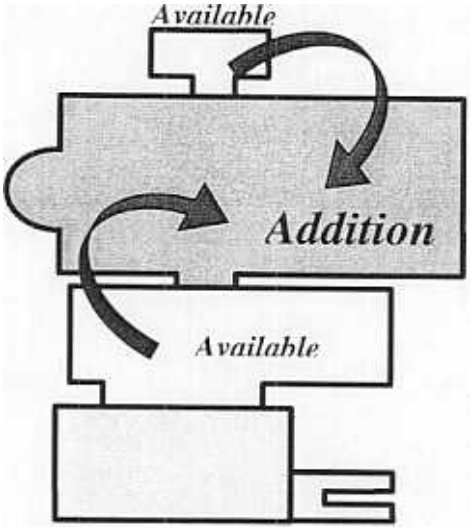


Only parts of the existing activities will fit into the addition. To minimize the adverse impact on operations, some areas in buildings 1425 will continue to be occupied. The area of Building 1425 that is vacated will become the first phase of existing space to be altered. As areas are vacated, they will need to be at least partially decommissioned (decontaminated prior to construction worker occupancy). There will be operational challenges since the alteration work will become a barrier between unrenovated existing

space and the new addition. Importantly, physical security will become more difficult as construction contract personnel will work in the space between active laboratories. During the extended period of construction additional personnel will be required for the security force.

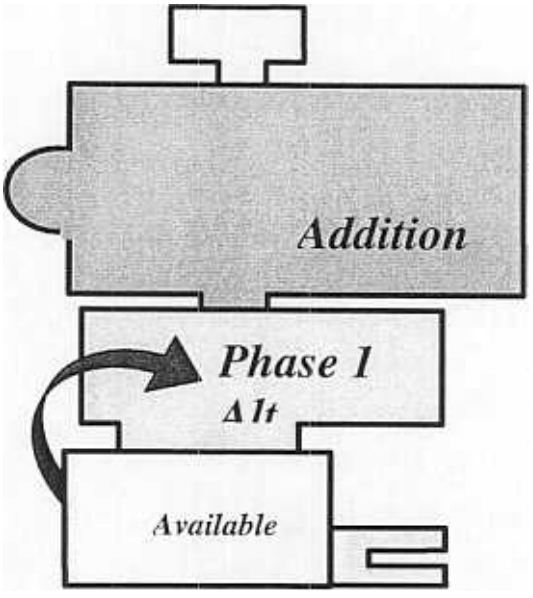
Upon completion of the Phase 1 Alteration, other activities currently in Building 1425 would be moved to the renovated section and the area, which these activities vacate, would become available for alteration. Again this will create a construction barrier between operating portions of USAMRIID. This will continue to pose a risk to laboratory security and require an increase to the security force. The existence of the construction barrier will also create inefficiencies due to split support operations. A detailed study will be required to develop a phased movement plan. It is probable that some operational elements may be required to move more than once.

Addition + Alteration-2



For example if glass wash operation is in the Phase I area, but will not be in the addition, then a temporary location may have to be constructed until the phase that does include glass wash is accomplished.

Addition & Alteration -3



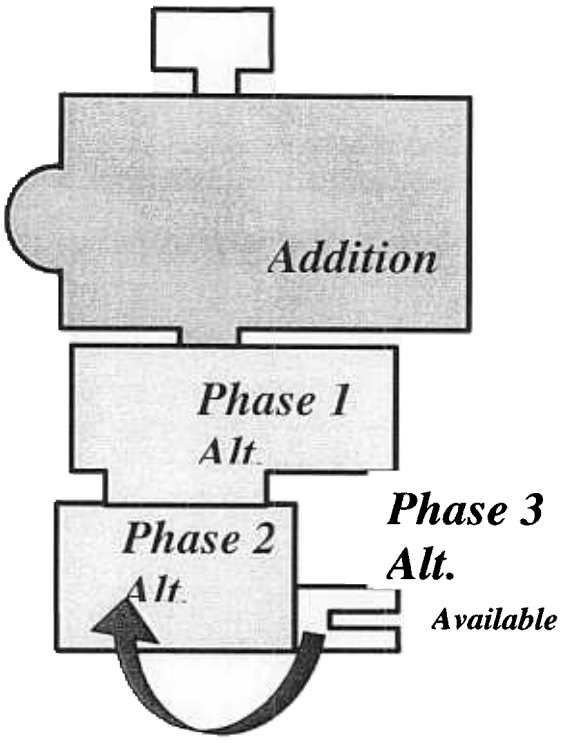
As in previous phases of the Addition + Alteration scenario, another portion of Building 1425 will become available for occupancy and another portion of the building will become available for alteration. In this last element of alteration work for the construction contractor, the area being worked on is somewhat isolated and does not create a barrier separating portions of the laboratory.

The last section of Building 1425 to be renovated is the area that houses the clinical trials (inpatient ward) and the contaminated patient care isolation

unit. These units are unique and for the period of time that this area is being renovated USAMRIID will be without this capability.

The construction of the addition for this scenario is projected to take 33 months. The operational impact associated with this portion of the construction work will create numerous security challenges and most likely require additional security force personnel. Following the construction of the addition, each of the alteration phases will take fourteen months to complete. Between each construction/alteration phase there will be a two-month period required to accomplish commissioning and the relocation/move of USAMRIID elements. Each of these moves posses an operational challenge to on-going research as well as a security challenge. In all, it is estimated that the Addition + Alteration alternative will require eight plus years to complete. Owing to the number of moves that will occur, a complex transition plan will be required. The execution of this alternative will be a greater drain on the USAMRIID operating budget since there will be more moving contracts, longer periods of disruption and a greater physical security cost.

Addition & Alteration-4

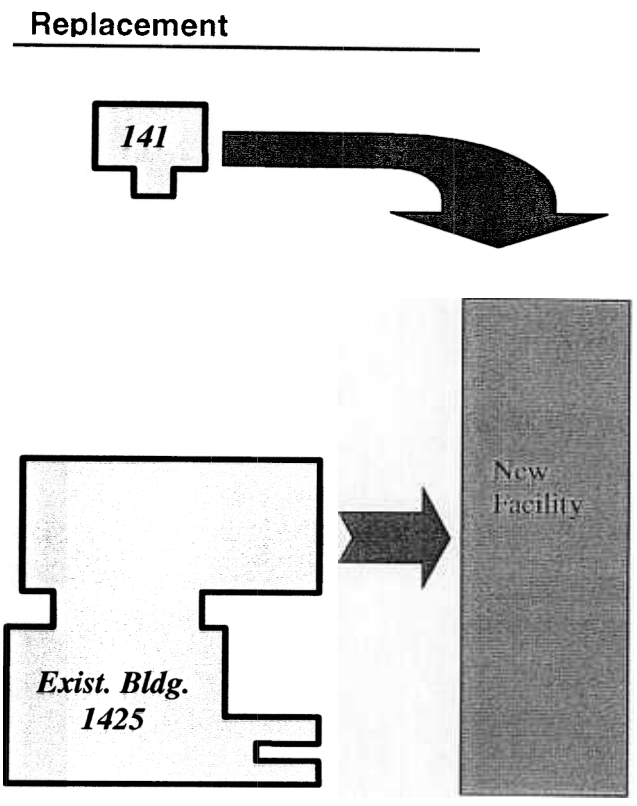


4.2.2 Replacement

The Replacement scenario vastly simplifies the impacts on current and future operations and is less costly. The new replacement building is constructed away from the existing laboratory. Security concerns during construction are minimized since the construction workers are not in the immediate area for current laboratory operations. Unlike the Addition + Alteration scenario, the likeihood of construction related interuptions to building services (electrical, water, etc.) is eleminated. Transition costs are minimized since there will be only one move and that will be directly to "final destination" locations in the new building. The risk of disruption to on-going research and the death of important biological samples is minimized. Since operations remain as they are until

relocation and construction personnel are separated from the laboratory, there should be no additional security force cost.

With the completion and commissioning of the replacement facility, USAMRIID operations would relocate from the old buildings to the new building. This move would be accompanied by a decompression of USAMRIID operations and an opportunity to hire needed researchers and support staff. The decommissioning of the old buildings could proceed in an orderly manner, unhampered by operational concerns.



The construction of the replacement facility associated with this scenario is projected to take 48 months. The operational impact associated with this portion of the construction work is minimal, since there will be physical separation of the laboratory from the construction site. The security impact and the impact on the operations budget of USAMRIID will be significantly less. The overall time associated with this scenario is four years or half of the addition + alteration scenario. This also means that USAMRIID can execute an expanded role in biological defense much sooner under this scenario.

5 Associated Costs

USAMRIID has a pressing need for facilities to appropriately house its current and future missions. Based on mission and staffing analysis, USAMRIID requires facilities of 1,150,200 gross square feet. Table 2 describes the cost build up to support the new USAMRIID. Costs for the Addition + Alteration scheme are only slightly lower that the total replacement costs shown here. Detailed cost data for each can be provided upon request.

PRIMARY FACILITY	Unit	Total Sq. Ft	Unit Cost	$553,796,667
Containment Laboratory Facility	SF	1,020,600	$490.84	(500,955,319)
Containment Animal Holding	SF	129,600	$386.79	50,127,348
Building Information Systems	LS	--	--	2,714,000
SUPPORTING FACILITIES				$141,259,000
Central Utility Plant	LS			(42,180,000)
Site Improvements	LS			(13,689,000)
Antiterrorism & Force Protection	LS			(31,919,000)
Systems Redundancy	LS			(53,471,000)
ESTIMATED CONTRACT COST				$695,055,667
CONTINGENCY PERCENT	5.0%			$34,752,783
SUBTOTAL				$729,808,450
SUPERVISION, INSPECTION &OVERHEAD	6.5%			$47,437,549
CATEGORY E EQUIPMENT				$48,981,000
TOTAL REQUEST				**$826,227,000**

Table 2. Supporting Cost Estimates for new construction for USAMRIID

This projected space is benchmarked to CDC space criteria standards as well as other like international laboratories. Detailed cost estimates for the project are available on request.

The following costs are estimated in addition to construction costs:

- Cost of facility design and studies (Environmental Analysis, Econ. Analysis) $100,000,000
- Costs of transitioning to the new building.....$66,000,000
- Costs of initial outfitting..... $14,000,000

None of the above estimates include increased organizational, personnel or operating costs.

6 Implementation into the Future Years Defense Plan (FYDP)

The requirement for replacement of USAMRIID has not been identified in the FYDP.

6.1 Plans for Implementation in the FYDP

Due to the urgent need for a replacement facility, an accelerated schedule for delivery is recommended. This accelerated schedule would allow for design to overlap with construction as shown in Figure 9. Design would start in FY 02 and be completed at the mid-point of FY 04. Construction on a site preparation package would begin at the beginning of FY 04.

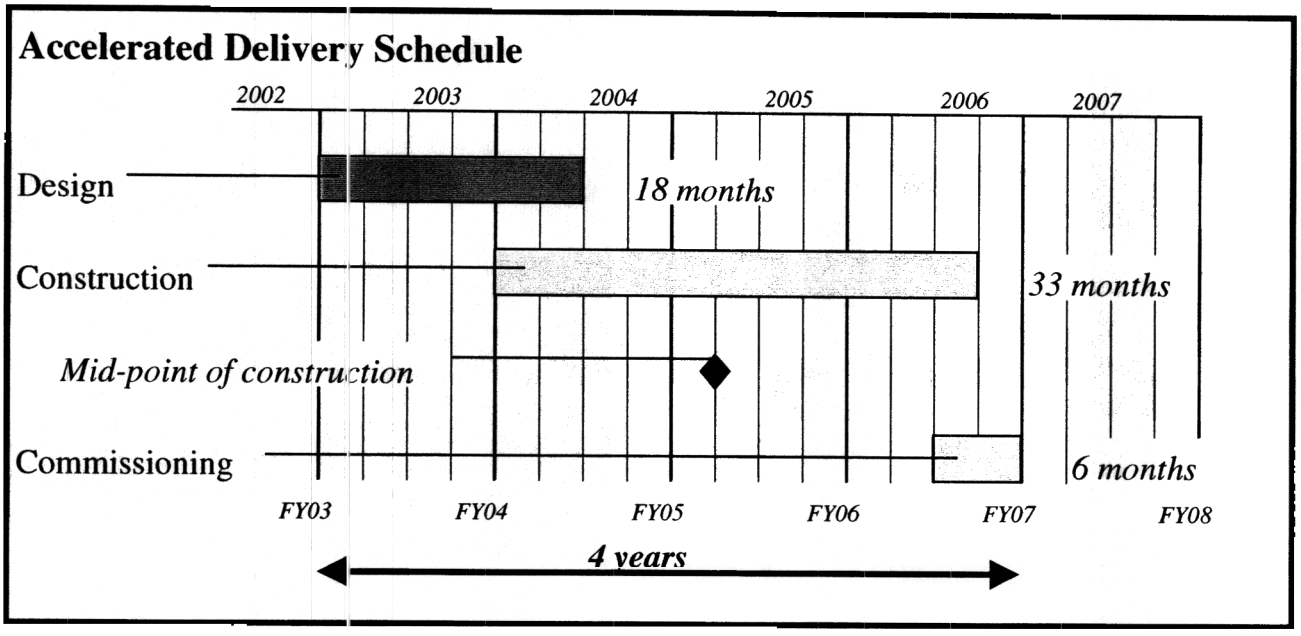


Figure 9. Accelerated USAMRIID construction schedule

6.1.1 Recommended Implementation of the FYDP

The recommended placement of funding for this project schedule is shown in Table 3. There are current projections for expansion of facilities for the National Institute of Allergy and Infectious Diseases, including a proposed BSL-4 facility to be placed at Fort Detrick. It may be possible to achieve an economy in satisfying the needs of both federal agencies (DoD and NIH) by evaluating what elements might be built in common, such as infrastructure for waste decontamination, animal care, logistics, security and others. The concept would be analogous to a consortium arrangement with co-located facilities that complement each other.

	FY03	FY04	FY05	FY06	FY07	TOTALS	Notes:
MLCCN	$100	$100	$300	$426		$926	FY03 - $100 Mis for design
Other Procurement				$2	12.0	$14	Outfitting Costs
Operations & Maintenance			10.0	20.0	$36	$66	Transition costs.
TOTALS	$100	$100	$310	$448	$48	$1,006	

Table 3. Future Years Defense Program implementation schedule. All Figures in $000

7 Summary and Conclusions

Few institutions are as important to our nation's biological defense as USAMRIID. Its work, especially with the ability to respond to the events like the anthrax incident has been central to the health of our Armed Forces and now more importantly that of the nation. No other institution has the capabilities or is positioned to meet potential threats posed by biological agents used as weapons of mass destruction. It has unique capabilities such as: a human BSL3 and BSL4 ward, aerosol testing in biocontainment, containment laboratory capacity, surge diagnostic capacity and FDA required challenge studies animal testing capacity. Very important to such research, USAMRIID is located on Fort Detrick in a community with a long history of support for medical research and accessible to the National Institutes of Health campus and other scientific and first response Federal agencies.

USAMRIID has a central role in the future of the nations expanding efforts in biological defense. It has strong existing ties to other federal and private biological research organizations. These collaborations will expand as almost many research entities depend on USAMRIID to fill needs which their respective organizations are incapable of providing. The CDC and NIH, especially NIAID are particularly strong partners with USAMRIID in the effort to provide a system of tiered laboratories for both the development of biological defense products and the identification of threat agents.

The facilities that currently house USAMRIID are inadequate due to age and capacity. The newest laboratory building which houses most of USAMRIID's containment laboratories in over thirty years old. It was constructed using the concepts, criteria and equipment current in the late 1960s. Every area of USAMRIID is overcapacity and borders on unsafe. Modern security and new requirements for anti-terrorism and force

protection make the existing infrastructure critically non-compliant. The current USAMRIID facility limits the dedicated staff in their important work.

Based on an analysis that compared USAMRIID's staffing and research workload to other biological laboratories, a larger, more capable replacement facility is urgently required. Due to the limitations of the existing facilities, the need to maintain current research efforts and the need to maintain security over the pathogenic agents, a renovation or addition and alteration project is not recommended, nor would it be the most cost or time effective solution to USAMRIID's facility problems.

Appendix A - Frequently Asked Questions about USAMRIID

What is USAMRIID's Mission?

USAMRIID fulfills a unique mission in support of both our armed services and our homeland security. The mission was established to conduct research on pathogenesis, diagnosis, prophylaxis, treatment, and epidemiology of naturally occurring infectious diseases of military importance with emphasis on medical defense against agents considered potential biological weapons, and highly pathogenic agents that require special biological containment. USAMRIID conducts research that leads to medical countermeasures including vaccines, therapies, diagnostics, and information to protect U.S. military personnel against biological threat agents.

This mission includes

- Primary bioterrorism laboratory response for the national capital area (NCA)
- Support to CDC as the only other "Level D" bioterrorism preparedness and response laboratory in the nation capable of handling agents such as smallpox or viral hemorrhagic fevers (Ebola, Marburg, etc.)
- A treatment facility including the only BSL-4 patient isolation ward in the U.S.
- Research and development of drugs and vaccines for highly pathogenic agents
- Laboratory personnel and expertise in support of the Defense Threat Reduction Agency's efforts to reduce the threat of spread of biological agents from the countries of the former Soviet Union.

Much of the facilities that support this mission are unique and are not duplicated anywhere in the U.S.

How does USAMRIID support military readiness?

USAMRIID provides direct support to military readiness in

- Diagnosing illness to troops stationed in foreign areas. For example, Crimean-Congo hemorrhagic fever is epidemic in Afghanistan and neighboring countries.
- Researching and developing drugs and vaccines for highly pathogenic agents that may be encountered by US armed forces.
- Providing patient isolation, medical evacuation, and medical care of service members that have developed diseases from highly pathogenic agents.
- Providing support and protection for service members encountering biological warfare or bioterrorism agents.

Can any functions or services provided by USAMRIID be out-sourced to private entities at less cost?

Due to the unique nature of the mission and the facilities required for its support, most functions cannot be out-sourced to private entities. However, some functions are already out-sourced or are considered "extramural" such as the continued clinical trials and development of drugs and vaccines.

What opportunities exist to consolidate medical research operations with other DoD medical research organizations?

Due to the unique nature of the mission and the facilities required for its support, USAMRIID cannot be consolidated with other DoD research organizations. There are no like units in the DoD. In addition, due to its high target potential as a bioterrorism preparedness and response laboratory, it should remain isolated from other similar laboratories to provide redundant capability for response. Note that at BSL containment, there is some redundancy with only one other laboratory (CDC in Atlanta).

What opportunities exist to consolidate medical research operations with other NIH medical research organizations?

The work of NIH and USAMRIID focus on two separate populations - the US civilian population and the warfighter respectively. Over the past year there has been a convergence of potential infectious disease threats to each population, the method of exposure, and the risk for each population varies significantly. Collaboration with the NIH is outstanding. NIH has a presence at Fort Detrick with it National Cancer Institute. Plans are progressing to place NIH's first BLS4 facility at Fort Detrick. There are several areas where collaboration will increase as research progress toward product testing and FDA approval.

Do any opportunities exist to capture revenues from customers on a reimbursable basis?

The only currently potential sources of reimbursable revenue come from the customers that utilize the Special Pathogens Sample Testing Laboratory (SPSTL), which conducts diagnostic analysis of unknown samples suspected of containing a biological threat agent. Potential customers for this service include the FBI, Secret Service, and other related federal agencies. The SPSTL has traditionally been a very minor part of the

mission of USAMRIID prior to September 11, 2001. The majority of the funding received by USAMRIID is derived from core DoD R&D funding.

Can some or all of the USAMRIID's work be shifted to universities?

There are several universities that have notable basic research programs with outstanding research scientists. The work in universities tends to be basic research. There are few institutions that have the necessary containment laboratory facilities, security, logistics support, animal facilities or ability to sustain operations. Containment laboratories that do exist are small. There is also significant concern about the dispersion and access to highly pathogenic agents at multiple locations.

How much space does USAMRIID currently occupy?

356,000 gross square feet at Fort Detrick (status quo). The facilities are 25 to 55 years old.

What is USAMRIID's current space requirement?

USAMRIID space needs have grown for several reasons. Natural growth of programs, increased complexity of scientific endeavors and technology, regulation of biomedical research including laboratory animal care regulations, newer engineering and space criteria changes, increase in complexity of building system components, new Anti-terrorism/Force Protection and other security requirements and a large increase in required animal care space all requiring a total of 1,150,000 gross square feet.

Does USAMRIID's new facility need to remain in the national capital area?

Yes. Due to environmental impact requirements and general public opposition to new high-level biological containment facilities such as USAMRIID, the facility should be developed at Fort Detrick, Maryland, where high level biological containment facilities have been housed since WWII.

Is it cost-effective to relocate USAMRIID to areas outside of the NCA?

No. For the reasons stated above, the facilities should be developed at Fort Detrick, Maryland. In addition, the existing facilities are unique and would be expensive to relocate and the role of USAMRIID in providing response to bioterrorism for the NCA requires close proximity to the NCA.

Appendix B - Glossary

AIT - Aeromedical Isolation Team - a unit of USAMRIID that can transport patients safely back to USAMRIID for care and treatment

AAALAC - Association for the Assessment and Accreditation of Laboratory Animal Care

Biosafety Level 1 - 4

BW - Biowarfare

CDC - Centers for Disease Control

DD Form 1391 - The basic programming document used to develop military construction projects

- DARPA - Defense Advanced Research Projects Agency
- DASD CBD - The Deputy Assistant to the Secretary of Defense for Chemical and Biological Defense

DOE Department of Energy

FDA - Food and Drug Administration

Future Years Defense Program (FYDP) - The official document that summarizes forces and resources approved by the Secretary of Defense.

Joint Vaccine Acquisition Program (JVAP)

Level D Diagnostic Reference Laboratory - Level D laboratory designation is the highest level of confirmatory biological diagnostic capability that possesses the expertise to definitively diagnose an unknown agent.

MBDRP - DoD's Medical Biological Defense Research Program

MIDRP Medical Infectious Disease Research Program

NCA - National Capitol Area

NIAID - National Institute of Allergy and Infectious Diseases.

NIH National Institute of Health

SPSTL - Special Pathogens Sample Testing Laboratory

USAMRIID - United States Army Research Institute of Infectious Diseases

USDA - United States Department of Agriculture